Allostatic Load and Medical Illness 3
Written Video Transcript

Okay. Well, let me stop at this point and open it up for some questions. I haven't really finished my tour of the PTSD abnormalities but I think this is a good time at least for me to take a breath and for you to ask any questions about anything that I've shown so far. Yes? [00:00.20.00] Wait for the mike.

Dr. Friedman, some of the abnormalities you mentioned appear to be associated with chronic stress while others appear to have been detected in those with PTSD. Do you believe that PTSD is a form of chronic stress [00:00.40.00] or do you believe that the two conditions differ in important way?

My answer is yes. I think both things. I think that—I mean there certainly is evidence suggesting [00:01.00.00] that there's a difference between a traumatic stressor and a severe unpleasant situation. We know that from the psychological data. I don't think that we've really demonstrated that yet in terms of the PTSD literature. I think the question [00:01.20.00] you're asking me, which is wonderful question, is really I think for me one of the real important areas for future research. So, I don't know. But my guess is that PTSD is more like chronic stress than it isn't. But there may be some very distinctive differences particularly in terms of the capacity of recovery of the organism which would mean [00:01.40.00] in terms of responsivity to treatment.

Depression has been shown to be associated with a number of medical problems. And you also say that depression [00:02.00.00] is associated with elevated HPA levels and depression itself again is associated with PTSD. Do you believe that depression and PTSD are the same or different with regard to their relationships to medical illness?

Again thank you for the—this is terrific. See, I [00:02.20.00] ran out of time but the questions are giving me a chance to say some of the stuff that I really want to say. I think that depression and PTSD have a very interesting relationship. Just clinically first of all, I mean we know from epidemiological research that number one, [00:02.40.00] people with PTSD have an 80% likelihood of having at least one other psychiatric disorder. And the psychiatric disorder that is most frequently associated with PTSD is depression. We know also as you mentioned that depression is a disorder associated [00:03.00.00] with elevated HPA activity. So, the question is are these two peas in a pod going by different names or is there a difference? And I think that there is a great deal of overlap between PTSD and depression not just clinically but also psychobiologically. My own belief—and I'm the only one that's saying this [00:03.20.00] so far—is I think that the major difference between PTSD and depression with regard to medical illness is the phasic, the reactivity that you see in PTSD which you don't see in depression. So that, you know, we know the paradigm—I mean you [00:03.40.00] expose a person who has PTSD to

some kind of traumatic reminder and he or she is going to have a massive surges of blood pressure, of pulse rate, of other kinds of physiological activity. That doesn't happen in depression. So, I think that the (path of) physiology of depression and PTSD where they—[00:04.00.00] my guess is that when the dust settles several years from now after these things have been adequately researched that that's really going to be the difference. So, going along with that one prediction would be that there will be a greater likelihood of some of these episodic cardiovascular problems [00:04.20.00] associated with PTSD than with depression. An area that I didn't get a chance to talk about would be in the immunological system. Again because the immunological system as with the cardiovascular—at least in chronic stress, it hasn't been researched in PTSD—has both tonic and phasic reactions. You have [00:04.40.00] in PTSD, what we see in chronic PTSD, we see immunosuppression. The people with PTSD seem to have impaired immunological capability. But expose a person with PTSD to a traumatic situation or even a stressful situation and he or she is going to have a massive episodic [00:05.00.00] immunological response which maybe, as I will develop later, may be responsible for these episodic disorders like rheumatoid arthritis, like fibromyalgia, like chronic fatigue syndrome, etc, that come in phases. So, I do think that there is an important difference between the two. So, thank you for the question. [00:05.20.00] Well, if there's no other questions I'm going to move on. Here's another area where there has been very little—there's been no research to my knowledge in PTSD, some in chronic stress. And I think that this is a very, very important area particularly [00:05.40.00] in terms of children. Because as I showed you earlier on, the elevated CRF in PTSD, the elevated HPA activity, suppresses the growth axis, suppresses a growth hormone through (sematistatin) and other mechanisms. [00:06.00.00] And one would predict—and no one has looked at this. They haven't even looked at it in chronic stress very much. One would predict that children who have been physically or sexually abused, particularly prior to critical growth periods, whether it's the early growth periods [00:06.20.00] early in life or later in terms of adolescent maturation, that they would be affected. You know, in pediatrics they talk about children that are a failure to thrive. They don't develop normally, they don't meet the normal developmental milestones both physically in terms of motor function, in terms of psychological function. [00:06.40.00] So, I really do believe that this is an important area that we need to collaborate with people in pediatrics. Because my guess is that kids with PTSD may be at a great disadvantage in terms of growth and maturation. And obviously if we understand it then we can begin to do [00:07.00.00] the various preventive and other kinds of interventions. Here's another very important area and this is the reproductive system. CRF inhibits [7:13] releasing hormone which is important for both (lutinizing) follicle stimulating hormone, both, [00:07.20.00] would produce etc., etc., etc. And there are a number of ways by which the system is suppressed both in males and females. And so another important area to consider is the reproductive—not just sexual functioning but particularly in females reproductive functioning. And we're--[00:07.40.00] pleased to say that we're doing a study out in the University of Hawaii right now following women through pregnancy. The prediction is that those women exposed to either chronic stress or PTSD are going to have more problems in terms of the pregnancy itself, infertility, spontaneous abortions, ectopic pregnancies, preterm contractions. [00:08.00.00] And also there's some—one study

suggesting that women with chronic stress or PTSD are more likely to have congenital malformations such as (neurotube, conotruncle) and, and other kinds of problems, cleft palate, etc. So, again, another important area that I think you don't even think about studying unless you think [00:08.20.00] in these terms of how might the psychobiology of PTSD affect certain important biological functions. Well, this is about the immunologic—this is about the metabolic system. And I'll be real quick here because I've got a lot of ground to cover. Essentially excessive CRH [00:08.40.00] will affect a number of metabolic activities including insulin resistance thereby making vulnerable to diabetes type two, lipid function, making people at greater risk for heart disease, hypertension [00:09.00.00] and other kinds of problems. Furthermore, particularly in women, bone mass, so osteoporosis. So, one again would predict that women—particularly women but males too. Actually there was a recent study with males, military men, who were exposed to—with PTSD [00:09.20.00] had (ostiopenia) and some osteoporosis which was associated with PTSD. So, again the data are starting to come in and they seem to be consistent with this way of thinking about things. So, again here's metabolic—it's called metabolic syndrome X. It's been shown in chronic stress. It hasn't been [00:09.40.00] looked at in PTSD. I predict if we look for it we're going to find it. Obesity, type two diabetes, atherosclerotic heart disease, ostiopenia, osteoporosis as well as clot formations, strokes, etc. [00:10.00.00] Okay here's another one, irritable bowel syndrome. We know clinically that irritable bowel syndrome, so called functional bowel disease, seems to be exacerbated by stress. And there's a very good biological reason why this might be the case. Elevated CRF is going to increase colonic motility, decrease gastric motility. Again [00:10.20.00] I'm just repeating myself so we'll move on. But again the model, the model makes all kinds of I think very interesting predictions with all kinds of medical complications—considerations. This is the immunological system and I'm going—I'm just going to skip over some of this because I'm just running late. But, as you can see [00:10.40.00] there are important reciprocal relationships between CRH and (cytokines) and other immunological markers. And as I said earlier, during the question period my reading of the literature—and again this is based primarily on the chronic stress literature. Although there's been some work with PTSD [00:11.00.00] and there's been three different groups, interesting groups. There's been military cohorts, there have been Israelis exposed to Scud attacks and there's a very interesting recent paper from Croatia on Croatian women that were incarcerated during the war with Serbia. And the data suggest again [00:11.20.00] that there's a chronic immunosuppression but re-exposure to stress can retrigger a phasic immunological reaction. And chronic immunosuppression the implications are increased [11:35] susceptability, delayed wound healing and some really interesting questions about whether [00:11.40.00] these folks would be at higher risk for cancer, AIDS, etc. Again, this is unmarked territory. But the theory would suggest at least it's worth a look, a serious look in these directions. And [00:12.00.00] you can read this—the stress—this is just a list of the variety of disorders that are episodic. They seem to be stress induced and I believe are related to PTSD. Again, the research has yet to be done although with the Persian Gulf cohorts it certainly does appear the fibromyalgia [00:12.20.00] and chronic fatigue syndromes seem to be to more prevalent among people with these disorders who were exposed to stress, irritable bowel syndrome, headaches etc. Okay. Now, allostasis

means stability through change and it is the way that the organism attempts to [00:12.40.00] maintain its balance in the wake of all the abnormalities that have been shown. Perhaps you can think about this if you're, if you're out in a canoe and the wind is blowing real hard you have to do some things in terms of rebalancing yourself to try to keep that canoe level, to keep yourself [00:13.00.00] from capsizing. Well in more complex way this is what the organism attempts to do. Previously we talked about this in terms of homeostasis but allostasis really takes into consideration how complicated these different systems really can be—and that you can have balances that may not be [00:13.20.00] at a homeostatic set point but can maintain the organism on relatively an even keel. But you pay a price and the price is what we call allostatic load. So, in order to maintain this kind of a balance there is wear and tear on the organism. There are other kinds of abnormalities that [00:13.40.00] take place. And this is what we're going to be talking about because I'm presenting allostasis, allostatic load as a way—as an unitary model that can incorporate, that can encompass all of the various system problems, changes, abnormalities that I've just rapidly illustrated [00:14.00.00] with regard to PTSD. Now, according to Bruce McKeown, who along with Elliot (Stellar) first coined the term allostatic load, there are four different ways that an organism can be out of balance. And these four different ways would make[00:14.20.00] —so that these are different solutions, different kinds of allostatic load solutions that the particular organism is making to his or her psychobiological abnormalities. And then we'll talk about the price that paid and the vulnerability to particular disease states that people might experience. [00:14.40.00] And we'll go through these again but one is—type one is repeated hits. Two is lack of adaptation, that the—normally when exposed to the same kind of a stress the organism learned how to habituate, how to cope with it so that a big initial response will become [00:15.00.00] diminished with time. And that's habituation, that's adaptation, it's very, very adaptive. There's a lot of evidence that suggest that people with PTSD can't do this. They can't adapt. And obviously that will have some consequences for health as well as for psychological status. [00:15.20.00] A third kind of allostatic load is a prolonged response that whereas following a stress there's a recovery period. These folks have lost the capacity to recover in a timely way. And a fourth type of allostatic load is an inadequate response. Now, when thinking about [00:15.40.00] allostasis what kind of tools, what kind of hardware, what kind of software does the body have to correct the imbalances? What kind of capacities I have to keep the organism's canoe from tipping in the high waves or the strong winds? Well, [00:16.00.00] a number of these are familiar. Certainly (gluco corticoids), DHEA which antagonizes gluco corticoids, I've talked about the [16:10], the different immunological agents the [16:13] a number of different hormones, thyroid hormone, insulin, insulin like growth factor which I didn't talk about [00:16.20.00] although it was on one of those previous slides which in addition to fostering growth seems to be a very important agent for neurogenesis, for growth of new neural tissue which has implications in PTSD. (Leptin) an important factor involved with fat deposition, obesity, etc and many of the pituitary [00:16.40.00] hormones ACTH growth hormone, etc. At the tissue level—so that's at the brain systemic level. At the tissue level there are again other kinds. And one of these tissues and perhaps the most important tissue is the brain. I've talked about CRF. [00:17.00.00] There are a number of amino acids particularly the NMDA, a glutibitergic system which

is involved both in learning, the fear conditioning that may be responsible for PTSD and also dissociation. Some of the abnormalities—you know some of the golden oldie neuro transmitters, serotonin or [00:17.20.00] (ephrneferin) and other neurotransmitters that have received less attention both in PTSD research and research in other psychological—psychiatric disorders. And again, I mean what I'm saying is there's a whole cast of characters so that there are many—the body has many different options [00:17.40.00] by which to correct allostatic load, by which to overcome it, though by which to leave the—keep the organism in some kind of balance. But obviously if you have to put out more neuropeptide Y to maintain some kind of a balance you're going to pay a price for that down the road. And that's really [00:18.00.00] the way we have to think about these things. The same thing is true with the immunological system etc. Now what are the factors that make that contribute to allostatic load and why might some people be more liable to developing PTSD? [00:18.20.00] We know that some people are more susceptible to PTSD. We know that even though in peacetime America roughly 50% of all men and women will have had at least one traumatic event only about 8% of them will have developed PTSD. So that means that the vast majority have somehow been able to [00:18.40.00] cope. Although as I showed you in an earlier slide that coping may come at a price. If you remember the slide of the sexually abused women without PTSD their HPA system was sensitized. It was not functioning normally. So that may be an allostatic [00:19.00.00] load that they're carrying around that would make them susceptible to developing PTSD or some other abnormality next time around. But clearly, you know, some of us are luckier than others, whether it's genetic risk for heart disease—some of us who can eat all of the red meat and vanilla ice cream [00:19.20.00] that we want and not raise our cholesterol levels. Well, the same is true in PTSD. Some of us have a genetic risk for developing PTSD when traumatized and some of us have a genetic loading for resilience, for being able to sustain such traumatic situations. And some of [00:19.40.00] this genetic risk for stress events as it plays out in terms of the medical scenario would be in terms of hypertension, diabetes. Okay, the second piece of this after you get to the genes is the (intrauterine) and neonatal [00:20.00.00] development. And again what happens while you're in utero may affect things later on. But we certainly know that abuse, particularly among neonates, may be a major risk factor not just for PTSD but for attention deficit disorder and other kinds of things. Because this kind of abuse is taking place, you know, [00:20.20.00] while the brain is still developing. And there is data to suggest that a young neonate who is subjected to abuse, that his or her brain is not going to develop in a normal way and there's going to be important complications. PTSD may be one of them. So, I'm talking about prenatal stress. Obviously childhood abuse is another important one. [00:20.40.00] Other kinds of factors having to do with depression, sleep deprivation, etc.—in other words what else is going on that might set the psychological and biological context on which the trauma [00:21.00.00] will be affecting you. Here is the area where we can make the most difference as clinicians because there are life style changes in terms of diet, in terms of taking care of oneself both physically as well as psychologically that can either increase our vulnerability [00:21.20.00] of developing PTSD and the consequences or can increase our resilience to cope with such situations. And another factor is we know that the effects of trauma are cumulative so that those women who had childhood sexual

trauma [00:21.40.00] but no PTSD, further sexual trauma or other kinds of trauma, military trauma, emergency room trauma etc, they appear to be at greater risk because already their [21:50] system is disregulated. It's not functioning at a normal level and so repeated stressful experiences may affect any of this stuff [00:22.00.00] in terms of cardiovascular function, in terms of brain function. There is data showing that people with PTSD have reduced (hippocampal) volumes so their brains are affected. We think we know why to some extent and immunological response. So, again there are a number of different ways to think about this. [00:22.20.00]

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